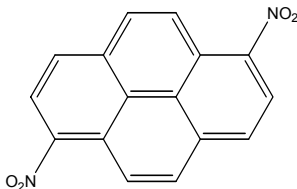


## NITROARENES (SELECTED)

### 1,6-DINITROPYRENE

CAS No. 42397-64-8

First Listed in the *Eighth Report on Carcinogens*



## CARCINOGENICITY

1,6-Dinitropyrene is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of malignant tumor formation in multiple species of experimental animals, at multiple sites and by multiple routes of exposure (reviewed in IARC V.46, 1989).

When administered by subcutaneous (s.c.) injections, 1,6-dinitropyrene induced injection-site sarcomas in male mice and male and female rats, and leukemia in female rats (Tokiwa et al., 1984, and Ohgaki et al., 1985; cited by IARC V.46, 1989; Imaida et al., 1995). Intraperitoneal (i.p.) injections of 1,6-dinitropyrene caused an increased incidence of liver-cell tumors in male mice (Wislocki et al., 1986; cited by IARC V.46, 1989) and induced sarcomas of the peritoneal cavity in female rats (Imaida et al., 1991b). Squamous cell carcinomas of the lung were induced in male rats receiving 1,6-dinitropyrene by intrapulmonary injection in two studies (Maeda et al., 1986; cited by IARC V.46, 1989; Iwagawa et al., 1989). The incidences of myeloid leukemia and lung adenocarcinomas were significantly increased in male and female hamsters receiving 1,6-dinitropyrene by intratracheal instillation (Takayama et al., 1985; cited by IARC V.46, 1989). 1,6-Dinitropyrene was found positive for carcinoma of the pituitary gland in an oral study of short-term duration in rats (Imaida et al., 1991).

There are no adequate data available to evaluate the carcinogenicity of 1,6-dinitropyrene in humans.

## ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Intratracheal administration of 1,6-dinitropyrene to rats previously inoculated to de-epithelialized trachea with an immortalized bronchial cell line, caused tumors when the tracheas were then implanted s.c. into nude mice (Iizasa et al., 1993). 1,6-Dinitropyrene is genotoxic in a wide variety of assays in bacteria and mammalian cells including human cells. 1,6-Dinitropyrene also demonstrates evidence of cell transformation activity in vitro in rat tracheal epithelial cells. Metabolic pathways leading to mutagenic and clastogenic metabolites and DNA adducts of 1,6-dinitropyrene have been described (IARC V.46, 1989).

No data are available that would suggest that the mechanisms thought to account for tumor induction by 1,6-dinitropyrene in experimental animals would not also operate in humans.

## PROPERTIES

1,6-Dinitropyrene occurs as light-brown needles when recrystallized from benzene and methanol. It can also be found as a yellow crystalline solid. It is moderately soluble in toluene and has a melting point of greater than 300°C. When heated to decomposition, 1,6-dinitropyrene emits toxic fumes of nitrogen oxides (NO<sub>x</sub>).

## USE

There is no evidence that 1,6-dinitropyrene has been used for other than laboratory applications. 1,6-Dinitropyrene is available for research purposes at ≥98% purity. It is also available in <sup>14</sup>C- or <sup>3</sup>H-labeled form at ≥98% radiochemical purity (IARC V.46, 1989).

## PRODUCTION

One foreign company synthesized >99.9% pure 1,6-dinitropyrene (IARC V.46, 1989). One American company produces 1,6-dinitropyrene (SRI, 1992), and Chem Sources identified three American suppliers (Chem Sources, USA, 1992). No data on imports or exports were available.

## EXPOSURE

The primary route of potential human exposure to 1,6-dinitropyrene is inhalation. Detectable levels have been found in ambient atmospheric samples. Higher amounts have been reported in heavy industrialized areas than in nonindustrialized urban and suburban sites. 1,6-Dinitropyrene has been found in various concentrations in extracts of particles from the exhaust of heavy-duty and light-duty diesel engines. It has also been found in small amounts in particulate emissions from kerosene heaters and gas burners. Prior to 1980, some carbon black samples known to be used in photocopy machines were found to contain considerable quantities of 1,6-dinitropyrene. 1,6-Dinitropyrene is not listed in the National Occupational Exposure Survey or the National Occupational Hazard Survey conducted by NIOSH.

## REGULATIONS

OSHA regulates 1,6-dinitropyrene under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-91.